In Vitro Testing of Engineered Nanomaterials in the EPA's ToxCast Program

Keith Houck

U.S. Environmental Protection Agency (EPA), National Center for Computational Toxicology, RTP, North Carolina, USA.

High-throughput and high-content screens are attractive approaches for prioritizing nanomaterial hazards and informing targeted testing due to the impracticality of using traditional toxicological testing on the large numbers and varieties of nanomaterials. The ToxCast program at the US EPA has used various high-throughput assays and developed computational tools to help assess potential toxicity and identify toxicity pathways of hundreds of traditional chemicals. We investigated the compatibility of selected ToxCast cellular, high-throughput screening assays on engineered nanomaterials, with the ultimate goals of identifying toxicity/biological pathways affected by nanomaterials and finding correlations among nanomaterial physicochemical characteristics, testing conditions, and nanomaterial toxicities/bioactivities. Au, Ag, CeO_2, $Cu(O_2)$, TiO_2, SiO_2, and ZnO nanoparticles, their ion and micro counterparts, carbon nanotubes (CNTs), asbestos, and pesticides containing nano-Cu(O) were screened at 6 -10 concentrations each. A total of 262 bioactivity/toxicity endpoints in cells and zebrafish embryos were measured. Cellular stress and immune response pathways were the most common pathways affected. NM's core chemical composition was more important than size for bioactivity. . Ag, Cu, and Zn (nano and ion samples) were the most active materials with nano and ion counterparts producing similar profiles, suggesting ion shedding was a key factor in mechanism of action. While 3 asbestos samples had similar immune response profiles, 6 CNTs had profiles distinctive from asbestos We demonstrated that HTS assays can identify affected cellular pathways, predict targets, and may be useful for ranking NMs for specific purposes. *This abstract does not necessarily reflect EPA policy.*